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EXAMINER	
SCHLAPKOHL, WALTER	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/763,712	DILLON, HARRISON F.	
	Examiner	Art Unit	
	Walter Schlapkohl	1636	wls

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2004 and 14 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *29-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28 and 40-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/28/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the papers filed 11/25/2004 in which claims 10 and 19 were amended and claims 40-41 were added. Claims 1-41 are pending. Claims 29-39 are withdrawn. Claims 1-28 and 40-41 are under examination in the instant Office Action.

Election/Restrictions

During a telephone conversation with Harrison Dillon on March 21, 2006, a provisional election was made with traverse to prosecute the invention of Group 26, claims 2-28 as drawn to SEQ ID NO: 26. Affirmation of this election must be made by Applicant in replying to this Office action. Claims 29-39 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see, e.g., page 34, line 15). Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences are set forth in the specification and drawings that lack sequence identifiers (see, e.g., page 2, line 27 of the specification and Figures 15-17). It is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 244.02). If the sequences are already present in the sequence listing, it would be remedial to amend the Brief Description of the Drawings to include the appropriate sequence identifiers as long as it is clear which sequence in the figure is identified by each sequence identification number included in the Brief Description of the Drawings. Applicants are required to comply with all of the requirements of 37 CFR 1.821 - 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F. R. 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

Claim Objections

Claims 3, 5, 11, 17, 26 and 40-41 are objected to because of the following informalities:

Claims 3, 11 and 26 contain non-elected subject matter.

Claim 17 recites "[t]he method of claim 1, wherein cell is of the genus Chlamydomonas" and should instead recite "[t]he method of claim 1, wherein [[the]] cell is of the genus Chlamydomonas."

Claims 5 and 40-41 contain sequences which lack sequence identifiers (see section entitled "Sequence Compliance" above).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 10 & 12, and therefore dependent claims 2-9, 11, 13-28 & 40-41, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "[a] method for engineering a cell to produce an increased amount of hydrogen comprising: (a) providing a mutagenized nucleic acid sequence derived from a first gene that encodes a protein involved in a hydrogen production pathway; (b) transforming a cell with said mutagenized nucleic acid sequence; and (c) screening or selecting the cell for an increased amount of hydrogen" in lines 1-6. Claim 1 is vague and indefinite in that the metes and bounds of a nucleic acid sequence "derived from a first gene" are unclear. What steps are involved in the deriving and which structural features/sequences are indicative of such a mutagenized nucleic acid?

Claim 10 recites "[t]he method of claim 5, wherein the mutagenized nucleic acid sequence is generated by a mutagenesis method described in U.S. Patents selected from the group consisting of 5,965,408; 6,171,820; 6,174,673; 6,238,884; 6,326,204; 6,344,328; 6,352,842; 6,358,709; 6361,97; 6,368,798; 6,440,668; 6537,776; and 6,605,449" in lines 1-4. Claim 10 is vague and indefinite in that it is unclear whether Applicant intends any method recited within the patents listed, or whether Applicant intends the patented method of mutagenesis from each of the recited patents.

Claim 12 recites "[t]he method of claim 4, wherein the mutagenized nucleic acid sequence encodes an iron hydrogenase protein that functionally interacts with a ferredoxin protein in the cell" in lines 1-3. Claim 12 is vague and indefinite in that the metes and bounds of the phrase "functionally interacts" are unclear. Does Applicant intend that an interaction, such than increased amounts of hydrogen production are attained or will any functional interaction between an iron hydrogenase and a ferrodoxin protein suffice?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The specification as originally filed does not provide support for the invention as now claimed: "[t]he method of claim 4, wherein at least one amino acid from the segment $X^1X^2X^3FX^4X^5X^6GGVMEAAX^7R$ and at least one amino acid from the segment ADX^8TIX^9EE are both substituted by a different amino acid in the protein encoded by the first gene in a gene reassembly reaction to generate the mutagenized nucleic acid sequence" (claim 40). Nor does the specification as originally filed provide support for the invention as claimed in claim 41: "[t]he method of claim 40, wherein more than one nucleic acid encoding at least a portion of the $X^1X^2X^3FX^4X^5X^6GGVMEAAX^7R$ segment and more than one nucleic acid encoding at least a portion of the ADX^8TIX^9EE segment are placed in the gene reassembly reaction, wherein more than one nucleic acid sequences encoding at least a portion of each segment contain distinct nucleotide sequences." The specification does not provide sufficient

blazemarks nor direction for the instant methods encompassed by the above-mentioned limitation, as currently recited. The instant claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Claims 1-28 and 40-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods for engineering a cell to produce an increased amount of hydrogen comprising: (a) providing a mutagenized nucleic acid sequence derived from a first gene that encodes a protein involved in a hydrogen production pathway; (b) transforming a cell with said mutagenized nucleic acid sequence; and (c) screening or selecting the cell for an increased amount of hydrogen. While

some claims are further limited to green algae cells and other claims are further limited to such a method wherein the gene that encodes the protein involved in a hydrogen production pathway is iron hydrogenase, none of the claims are limited to green algae cells comprising a first gene that encodes an iron hydrogenase. Thus, the claims encompass any cell and/or any gene that encodes a protein involved in any hydrogen production pathway such that the gene can be mutated and the cell can be screened and, ultimately, engineered to produce an increased amount of hydrogen. The claims do not provide any structural information with regard to the gene sequences or cells capable of use in a method such that the gene can be mutated and the cell can be screened and engineered to produce an increased amount of hydrogen. Thus, the rejected claims comprise a set of nucleic acid sequences and cells that are defined by their function.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification

describes the use of *Chlamydomonas reinhardtii* (strain cc-400) which have been transformed with mutagenized (shuffled) nucleic acids derived from iron hydrogenase as well as five other genes which are differentially expressed in cells cultured under conditions conducive to the generation of hydrogen and cells cultured under conditions not conducive to the generation of hydrogen (pages 39-46). The specification also describes such a procedure for hydrogenase-ferredoxin chimeras (see Example 2, pages 47-51). The specification also describes a chemochromic screening method wherein colonies that produce hydrogen induce dark spots on chemochromic film directly over the colony (page 46). The specification further describes the isolation of DNA from iron hydrogenase-ferredoxin chimera colonies exhibiting the highest level of hydrogen production (page 50). This DNA is amplified and the resulting hydrogenase-ferredoxin secondary test constructs are transformed back into *C. reinhardtii* and screened (pages 50-51). No description is provided of any cell other than a *C. reinhardtii* cell in which this method is performed. No description is provided of any genes other than iron hydrogenase-ferredoxin chimeras which were capable of inducing *C. reinhardtii* cells (or any other cells) to produce increased amounts of hydrogen after mutagenization and transformation into the cells.

Even if one accepts that the examples described in the specification meet the claim limitations of the rejected claims with regard to structure and function, the examples are only representative of one chimeric gene sequence transformed into one kind of cell such that the cell was engineered to produce an increased amount of hydrogen. The results are not necessarily predictive of any other gene sequences used in combination with any other type of cell such that the transformed cell produces increased amounts of hydrogen. Thus it is impossible to extrapolate from the example(s) described herein those nucleic acid molecules and those cells that would necessarily meet the structural/functional characteristics of the rejected claims.

The prior art does not appear to offset the deficiencies of the instant specification in that it does not describe a set of genes or cells that can be used in a method for engineering a cell to produce increased amounts of hydrogen. Ahmann (Combinatorial Mutagenesis of a Bidirectional Hydrogenase in Chlamydomonas reinhardtii, National Science Foundation Grant No. AWSFL008-DS3, 2002) describes such a method comprising the use of *C. reinhardtii* cells transformed with mutagenized iron hydrogenase, but Ahmann does not teach such a method with any other genes or cells. Moreover, Ghirardi et al (Trends in Biotechnology, 18(12):506-511, 2000) teach that "[h]ydrogen (H_2)

metabolism is primarily the domain of bacteria and microalgae" (page 506, first column, first paragraph). Ahmann also teaches that the production of H_2 based upon the activity of hydrogenases "is restricted to green algae such as *Chlamydomonas reinhardtii*, which evolves H_2 from H_20 using an hydrogenase-based catalyst system with much greater potential energetic efficiency than other known systems" (see section entitled "Photosynthetic H_2 production" of the Introduction).

Given the very large genus of nucleic acid molecules and cells encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the genes and cells capable of fulfilling the claim limitations of claims 1-28 and 40-41, the skilled artisan would not have been able to describe the broadly claimed genus of cells and/or genes that encode a protein involved in any hydrogen production pathway such that the gene can be mutated and transformed into the cell so that the cell is screened, and ultimately, engineered to produce an increased amount of hydrogen. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those genes used in combination with those cells that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have reasonably

concluded Applicant was not in possession of the claimed invention for claims 1-28 and 40-41.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-4, 12-13, 15-21, 24 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Ahmann (Combinatorial Mutagenesis of a Bidirectional Hydrogenase in Chlamydomonas reinhardtii, National Science Foundation Grant No. AWSFL008-DS3, 2002) and as evidenced by Melis (*International Journal of Hydrogen Energy* **27**:1217-1228, 2002).

The exact date by which the Ahmann research proposal was available to the public is not clear. Applicant's IDS puts the date as 21 Feb 2002. The NSF website indicates the award was granted on 1 February 2002 (please see attached printout from the NSF website). In either case, the Ahmann document should have been available to the public before Applicant's effective filing date for claims 1-4, 12-13, 15-21, 24 and 26: 11/4/2002.

Ahmann teaches methods for the combinatorial mutagenesis of iron hydregonase genes obtained from a variety of different microorganisms and for the screening and selection of host cells comprising the resulting mutants for an increased ability to produce hydrogen (see entire document, especially "Statement of purpose section" of the Introduction). Regarding claim 2, Ahmann teaches such a method wherein a plurality of mutagenized nucleic acid sequences are used to transform a population of cells (ibid). Regarding claims 3-4, Ahmann teaches such a method wherein the first gene encodes an iron hydrogenase (ibid and Table 1). Regarding claim 12, Ahmann does not explicitly teach such a method wherein the mutagenized nucleic acid sequence encodes an iron hydrogenase protein that functionally interacts with a ferredoxin protein in the cell, but any mutant iron hydrogenase which results in increase hydrogen production must inherently interact with a ferredoxin protein in order for the hydrogen to be produced as evidenced by Melis, who teaches that "[l]ight absorption by the photosynthetic apparatus is essential for the generation of molecular hydrogen, since light-energy facilitates the endergonic transport of elections to ferredoxin" and that "[p]hotosynthetic ferredoxin is the physiological electron donor to the [Fe]-hydrogenase and, therefore, links the soluble [Fe]-hydrogenase to the electron

transport chain in the green alga chloroplast" (page 1218, first column, second full paragraph). Regarding claim 13, Ahmann teaches such a method wherein the screening or selecting occurs in the presence of oxygen at a concentration selected from the ranges comprising more than 0.5% (20-100%) (see section 5 of the Plan of Work). Regarding claim 15, Ahmann teaches such a method wherein the mutagenized nucleic acid sequence is generated by gene reassembly (see, e.g., section entitled "Combinatorial mutagenesis" of the Introduction). Regarding claims 16-17, Ahmann teaches such a method wherein the cell is of the genus *Chlamydomonas* (see, e.g., section 2 of the Plan of Work). Regarding claims 18-20, Ahmann teaches such a method wherein the sequences are retrieved from colonies showing increased hydrogen production, reshuffled and screened (see, e.g., "Statement of purpose" section of Introduction). Regarding claim 21, Ahmann teaches such a method wherein the screening or selecting occurs by culturing cells in liquid growth media (see, e.g., section 5 of the Plan of Work). Regarding claim 24, Ahmann teaches such a method wherein the mutagenized nucleic acid sequence is operably linked to promoter that is constitutively activated (see, e.g., Section 3 of the Plan of Work).

Conclusion

No claim is allowed.

Certain papers related to this application may be submitted to the Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is (571) 273-8300. Note: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Walter Schlapkohl whose telephone number is (571) 272-4439. The examiner can normally be reached on Monday through Thursday from 8:30 AM to 6:00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Walter A. Schlapkohl, Ph.D.
Patent Examiner
Art Unit 1636

July 20, 2006

NANCY VOGEL
PRIMARY EXAMINER